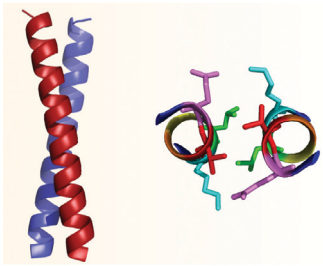
ACS chemical biology

In this ISSUE

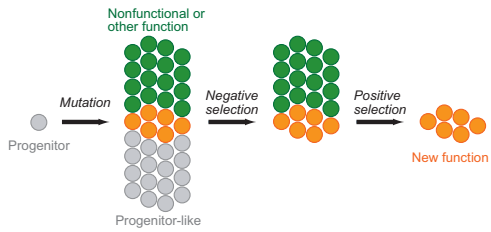
Synthesizing Cells from the Bottom Up



A completely artificial life system might be out of a page of a science fiction novel, but maybe not for long. Synthetic biology proceeds toward the goal of synthesizing new functionality often by reducing complex systems into simpler parts. On page 38, Bromley and colleagues discuss the challenges of creating synthetic biology systems by resolving the complexity and divergence of individual components. The authors delineate various hierarchical degrees of complexity that form into self-organized functional biological systems. The authors also provide specific suggestions with respect to the design of peptides with the possibility of using the α-helical coiled-coil structural framework to engineer both novelty and complexity. Using a similar bottom-up approach, synthetic biologists might one day be successful in creating intricate and unique biological systems. In addition, they discuss encapsulation systems that facilitate the biological requirement of compartmentalization.

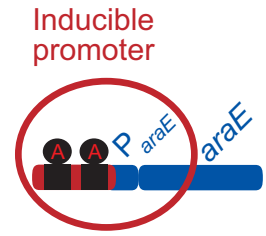
Building Pathways One Part at a Time

A point to consider while engineering an artificial process in a cell is that the cell must retain its own metabolism in order to survive. Filipovska and Rackham discuss this and other important observations in a "how-to" for building a parallel metabolism (p 51). The authors present the concept of the "module", a discrete entity that has a single biological function. They then describe how modules that are unrelated can work in parallel inside cells. The authors elucidate how these parallel modules can be evaluated by using techniques such as genetic screening and selection. The authors also describe the concept behind using orthogonal modules though a number of case studies, including reengineering of translation and reprogramming of the genetic code.

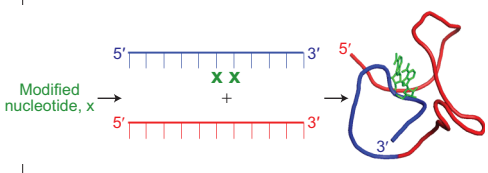


Engineering Cellular Complexity

Often, it is cheaper and easier to engineer cells to produce high-quality products than it is to make these products through organic total synthesis. On page 64, Jay Keasling discusses many of the benefits of creating metabolic pathways for synthesizing desirable products in single cells. Keasling compares key differences between metabolic engineering workflows and the overexpression methodologies currently used by the pharmaceutical industry. He observes that biologists, chemists, and engineers need to standardize the parts required to effectively build a biological system. These parts could be used to design, test, optimize, and implement integrated large-scale biosynthetic units. Keasling also discusses key process workflows in a synthetic biology system, including the development of core chassis, genetic control circuits, and simulation and debugging routines. The author also provides a concrete example of how many of these principles were used to engineer the production of the antimalarial drug artemisinin. This review explains that it is essential to use well-defined parts when engineering biological systems.



Tweaking RNA



Although modified nucleotides are known to be present in naturally occurring RNA, there is still much to be learned about what roles these modifications play in different contexts and in different cells. It is likely that the specific differences in structure and chemical reactivity that result from modifications play crucial roles in many cellular functions ascribed to RNA. Until very recently, a severe limitation in the study of natural and unnatural modifications was the lack of practical methodologies for generating modified nucleotides that could be incorporated in site-specific manner. On page 30, Chow and colleagues review the state of the art in the synthesis and incorporation of modified nucleotides into RNA. The authors note that a greater knowledge of the biological functions of modifications of RNA might be possible through design, synthesis, and analysis of modified nucleotides. The authors discuss chemical, enzymatic, and semisynthesis approaches, as well as techniques for generating modified RNAs containing thousands of nucleotides.

Published online January 18, 2008 • 10.1021/cb700266u CCC: $40.75